Kidney disease in hypertension

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Case I.

- 76 year-old woman
- History of hypertension (for 40years), type 2 diabetes on diet, MI (2x), stroke 1x
- Multicombination antihypertensive therapy, statins
- BP 150/95mm Hg
- S-crea : 1.6 mg/dl
- Urine: protein +1, no erythrocytes, proteinuria 0,9g/day
- Ultrasound: bilateral kidney 80mm, cortex 7mm

- What nephropathy does the patient have?
- What else could she have?
- What examination would you recommend?
- How would you treat the patient?

Case II.

- Woman 40 years
- Sudden unset of severe hypertension – 190/100, normal urea and creatinin, normal urine
- Therapy with perindopril in dose 10mg started, Ca blocker (amlodipin 10mg) and BB (metoprolol 100mg) added
- After 2 months – BP 110/60, urea 16mmol/l, creatinin: 4mg/dl
- Ultrasonography: asymetry of kidneys (R 85mm, L 108mm)

- What type of hypertension did the patient obviously had?
- What was wrong in the diagnostic process?
- What was wrong in the therapy?
- What examination would you recommend?
- What treatment?

Kidney's Role in BP Regulation

- Pressure Natriuresis
  - Regulation of salt and water
  - Vasopressin, Natriuretic Peptides
- Renin-Angiotensin-Aldosterone System
- Renal Sympathetic Nervous System
- Regulation of Vasoactive Hormones
  - Endothelins
  - Prostaglandins
- Nephron Mass

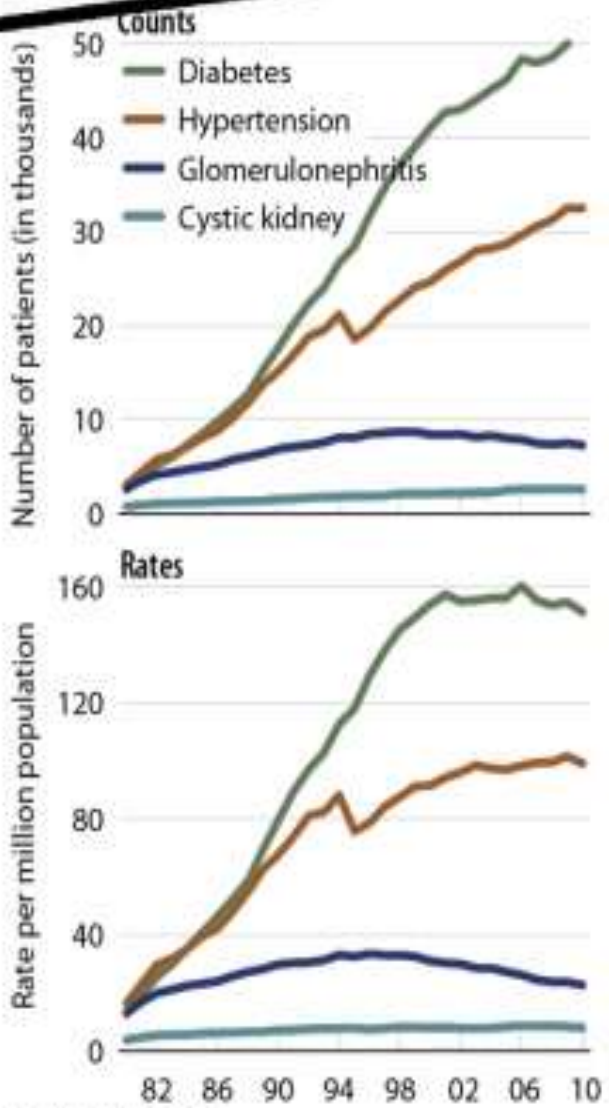
"the kidney is involved in the genesis of any type of hypertension" A Guyton


THE OLD CHICKEN AND EGG PROBLEM ...
SMACK
WHUMP
1
2
GOLDLAKE@GMX.NET

Kidneys ↔ hypertension

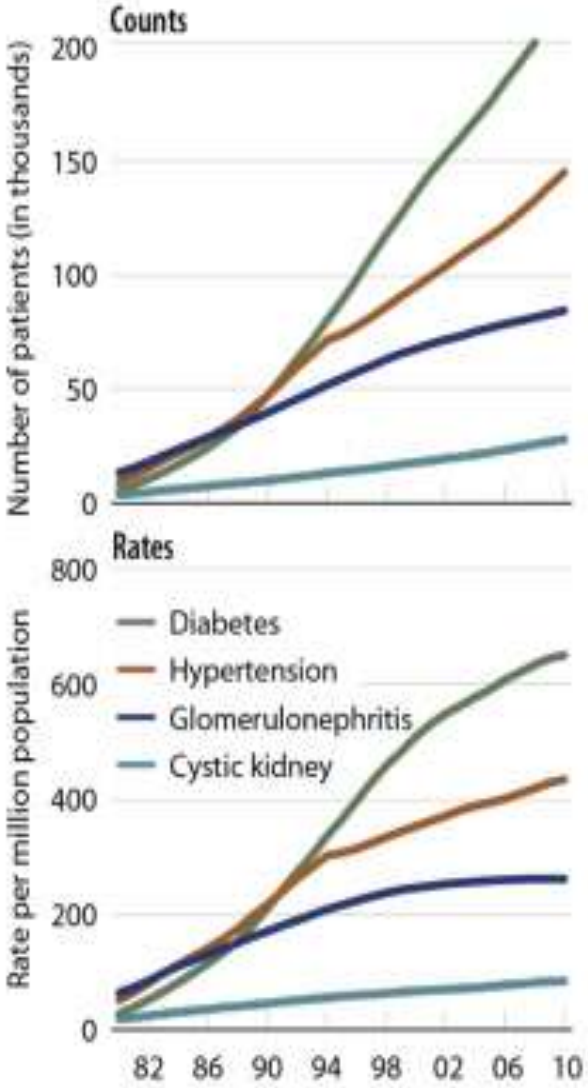
- role of kidneys in primary hypertension (inability to excrete salt load)
- kidney disease as cause of secondary hypertension (renoparenchymal, renovascular)
- hypertension causes renal damage
- hypertension is the leading factor of progression of kidney disease

Hypertension: 2nd Most Common Cause of ESRD



Incident ESRD

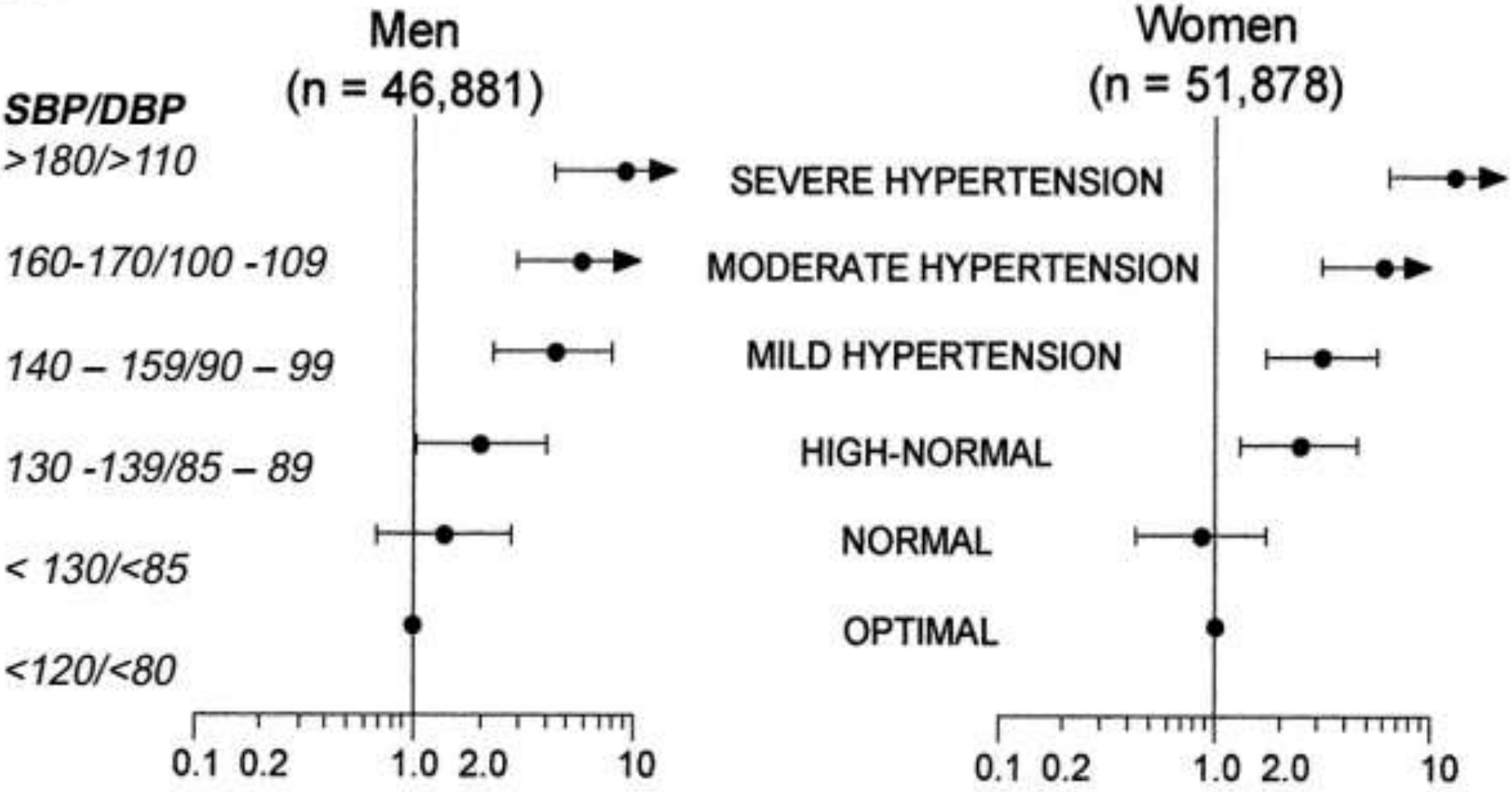
Adj: age/gender/race.



Prevalent ESRD

Adj: age/gender/race

ESRD Risk by Hypertension Stage



Tozawa M et al. Hypertension 2003;41:1341-1345

Hypertension Linked to ESRD

LECTURES

ON THE

PATHOLOGY, DIAGNOSIS, AND TREATMENT OF BRIGHT'S DISEASE.

By GEORGE JOHNSON, M.D., F.R.S.,
Physician to King's College Hospital; Professor of Medicine in King's College, London; etc.

LECTURE III.—CHRONIC BRIGHT'S DISEASE.

Small Red Granular Kidney.—Synonyms.—Outward Appearance of the Kidney in different Stages.—General History of the Disease.—Chemical and Microscopical Characters of the Urine.—Microscopic Appearances in the Kidney.—The Structural Changes are essentially tubular and intratubular.—Changes in the Blood-vessels of the Kidney.—Physiological Explanation of the Structural Changes in the Kidney and of the Condition of the Urine.

Definition

- The term ***hypertensive nephrosclerosis*** has traditionally been used to describe a clinical syndrome characterized by long-term essential hypertension, hypertensiveretinopathy, left ventricular hypertrophy, minimal proteinuria, and progressive renal insufficiency. Most cases are diagnosed based solely on clinical findings.

Aetio-Pathophysiology

Hypertension and Kidney Disease: A Deadly Connection

Yousri M. Barri, MD

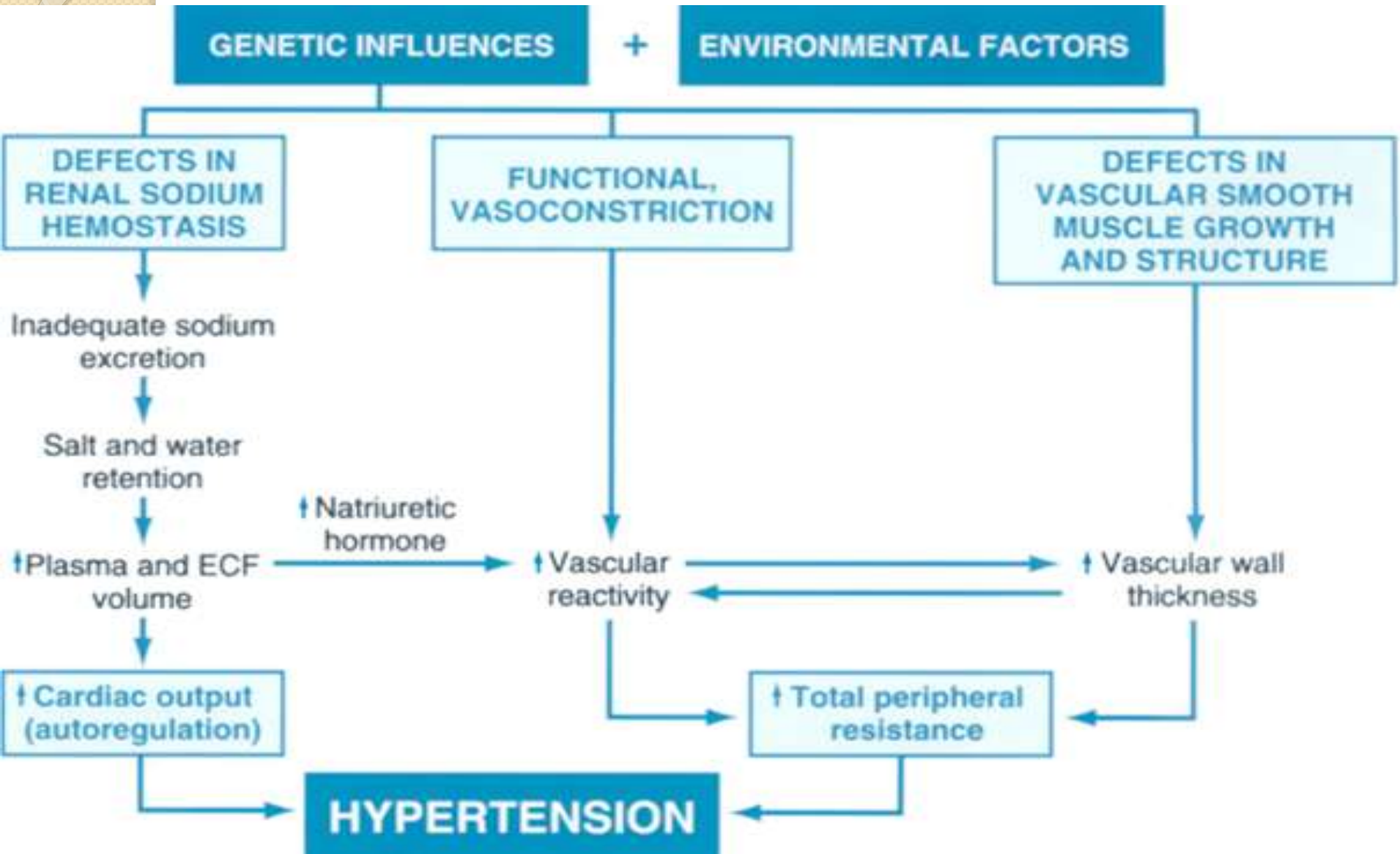
Table 1. Risk factors for hypertensive nephrosclerosis

African ancestry
Severe and long-continued hypertension
Family history of hypertension causing renal disease
Microalbuminuria
Diabetes mellitus
Left ventricular hypertrophy

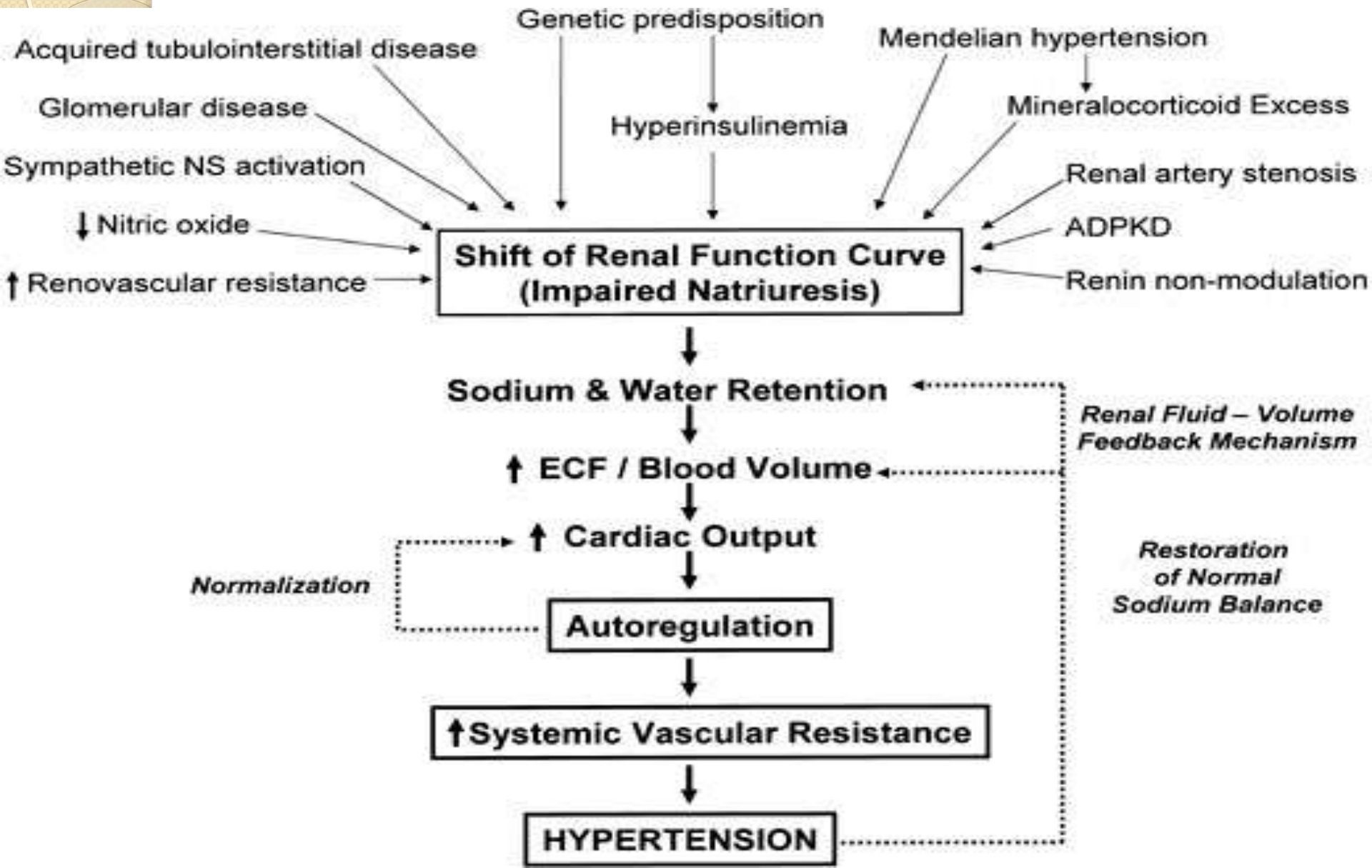
Genetics

- In 2008, 2 separate groups showed strong association between genomic variants within MYH9 (non–muscle myosin heavy chain 9) on 22q and nondiabetic ESRD in African Americans.
- The 2 other disease entities associated with MYH9 included HIV nephropathy and focal segmental glomerulosclerosis (FSGS) in African Americans.
- In 2010, 2 other groups showed an even stronger association between the ***APOL1* gene** and risk of ESRD in African Americans
- ACE gene (DD genotype) in African Americans.

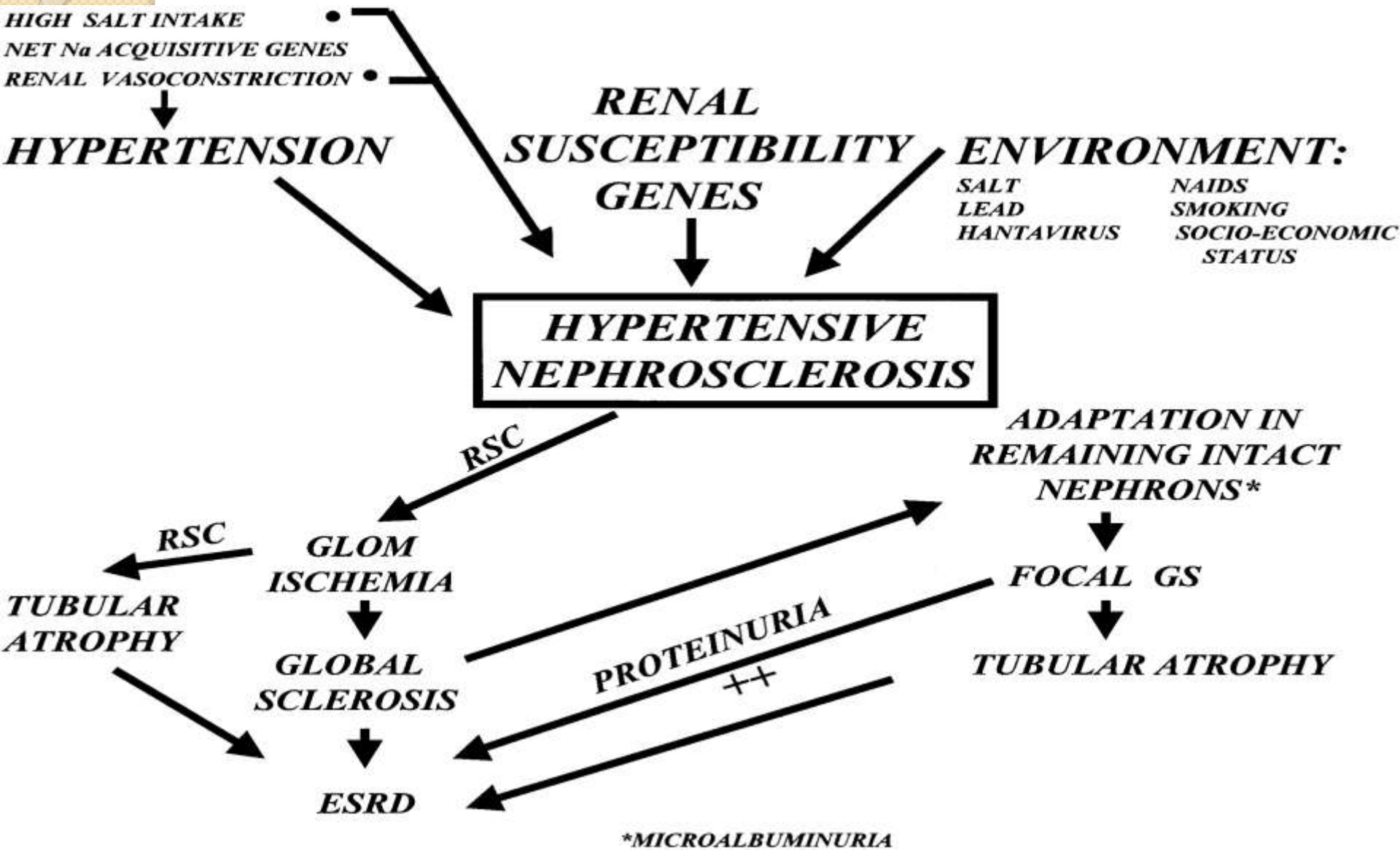
Kidney----→HTN


GENETIC INFLUENCES
+
ENVIRONMENTAL FACTORS
DEFECTS IN RENAL SODIUM HEMOSTASIS
FUNCTIONAL, VASOCONSTRICTION
DEFECTS IN VASCULAR SMOOTH MUSCLE GROWTH AND STRUCTURE
Inadequate sodium excretion
Salt and water retention
↑Plasma and ECF volume
↑Natriuretic hormone
↑Vascular reactivity
↑Vascular wall thickness
↑Cardiac output (autoregulation)
↑Total peripheral resistance
HYPERTENSION

Kidney----→HTN


Genetic predisposition
Acquired tubulointerstitial disease
Mendelian hypertension
Glomerular disease
Hyperinsulinemia
Mineralocorticoid Excess
Sympathetic NS activation
Renal artery stenosis
↓ Nitric oxide
ADPKD
↑ Renovascular resistance
Shift of Renal Function Curve
(Impaired Natriuresis)
Renin non-modulation
Sodium & Water Retention
Renal Fluid – Volume
Feedback Mechanism
↑ ECF / Blood Volume
↑ Cardiac Output
Restoration
of Normal
Sodium Balance
Normalization
Autoregulation
↑Systemic Vascular Resistance
HYPERTENSION

HTN--→Renal parenchyma



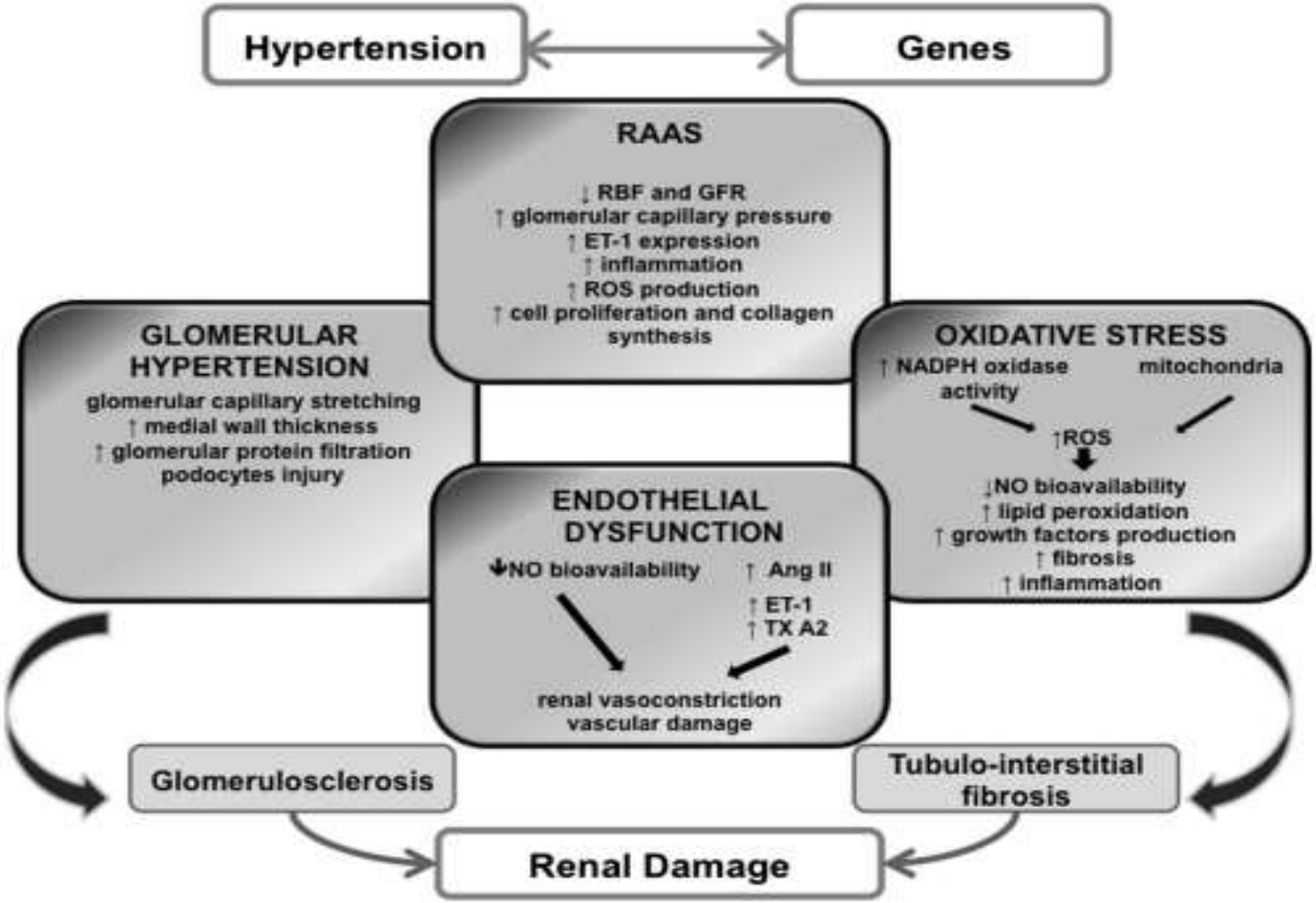
Journal of Human Hypertension (2014) **28,** 74–79

www.nature.com/jhh

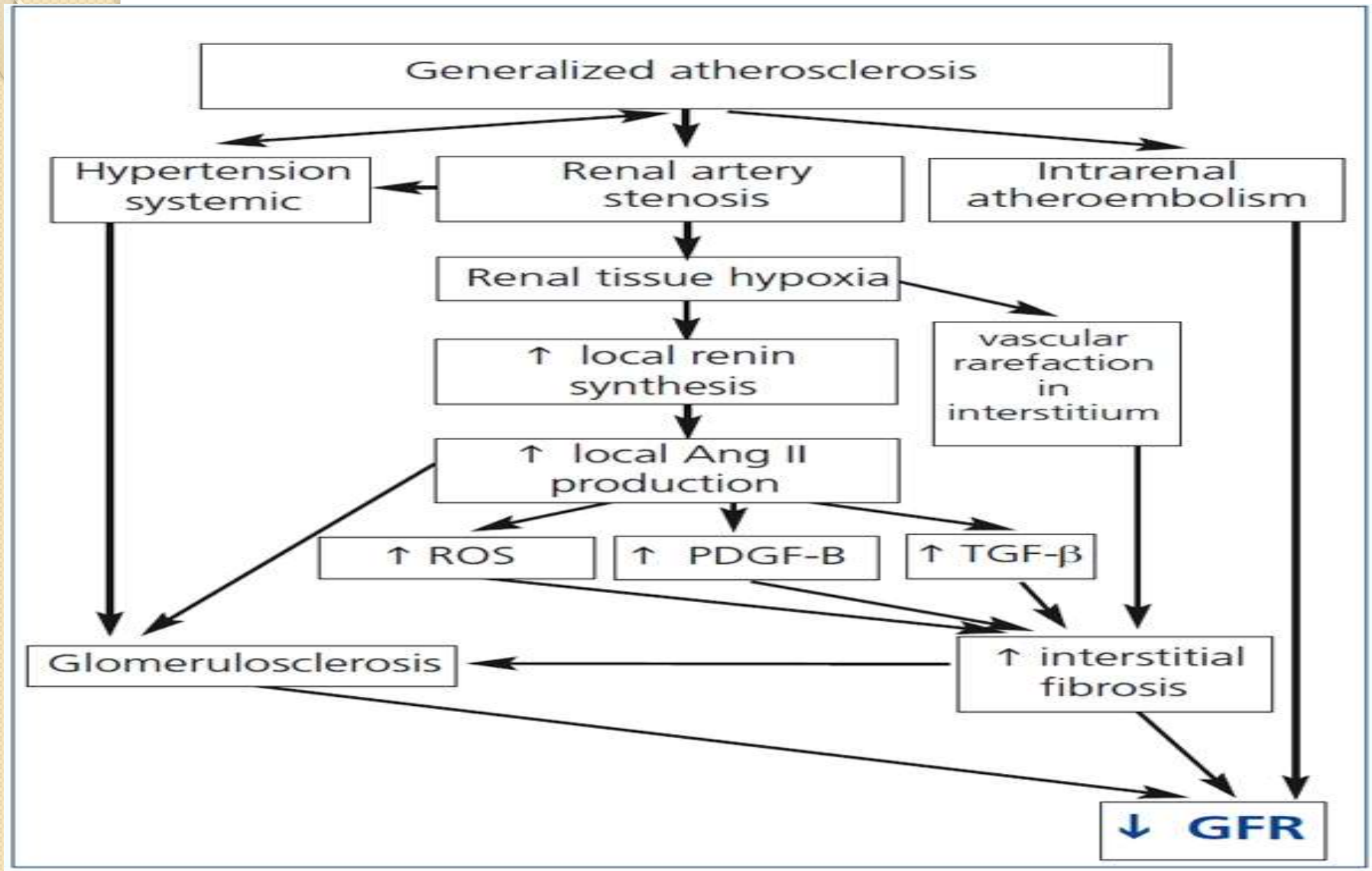
REVIEW

Hypertension and kidneys: unraveling complex molecular mechanisms underlying hypertensive renal damage

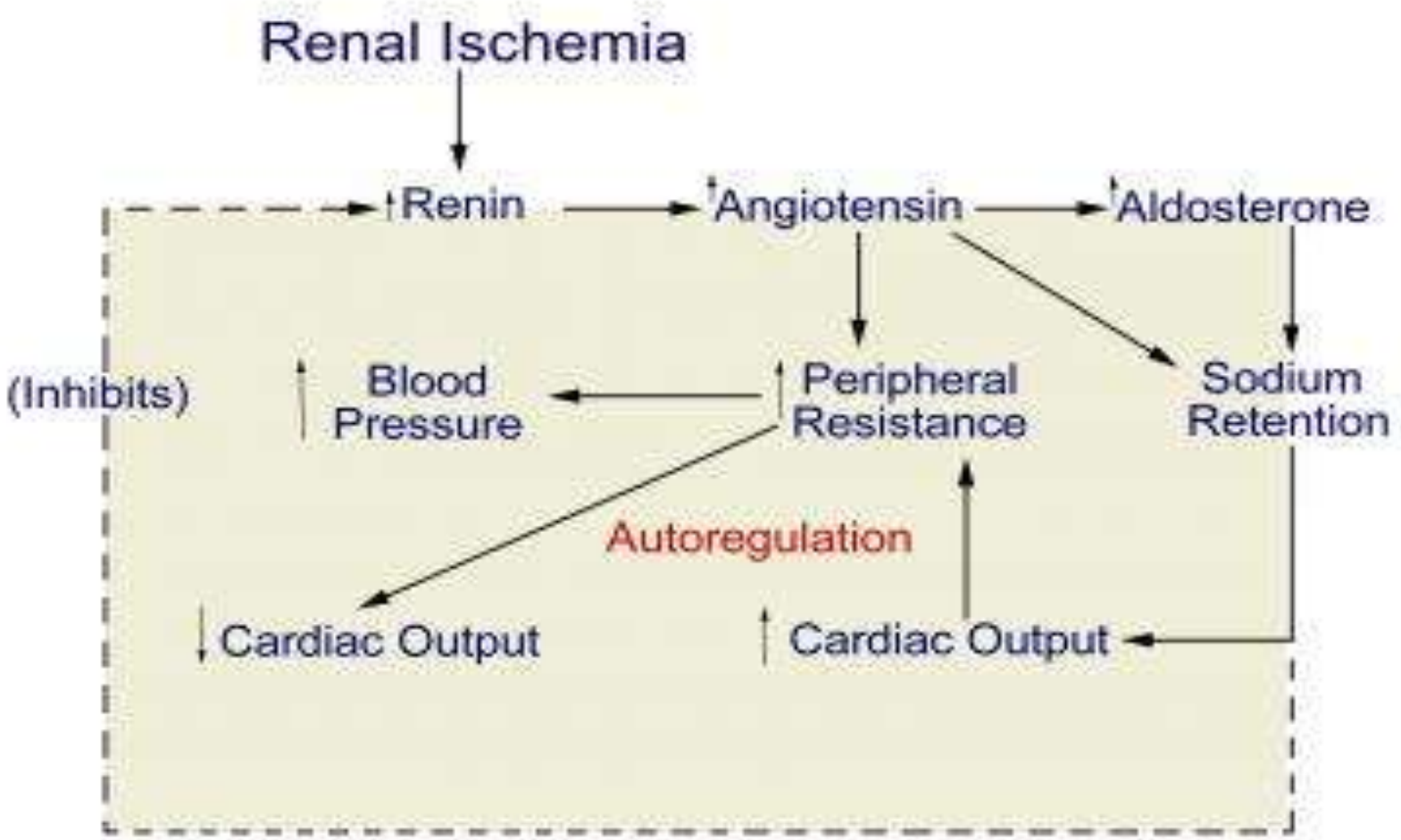
S Mennuni[1], S Rubattu[1,2], G Pierelli[1], G Tocci[2], C Fofi[3] and M Volpe[1,2]



HTN----→ Renal vessels



HTN----→ Autoregulation



Pathophysiology of Hypertensive Renal Damage

Implications for Therapy

Anil K. Bidani, Karen A. Griffin

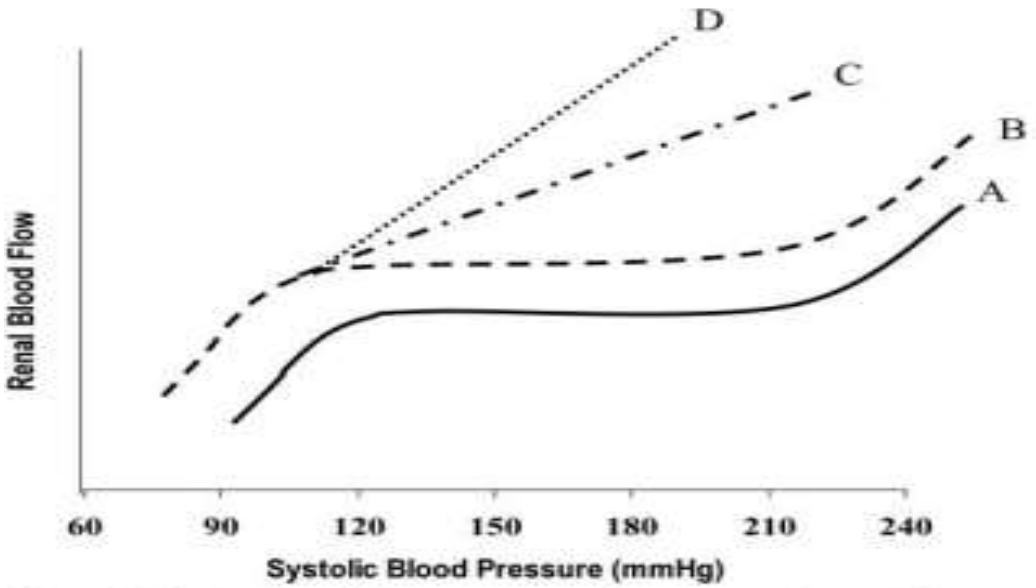
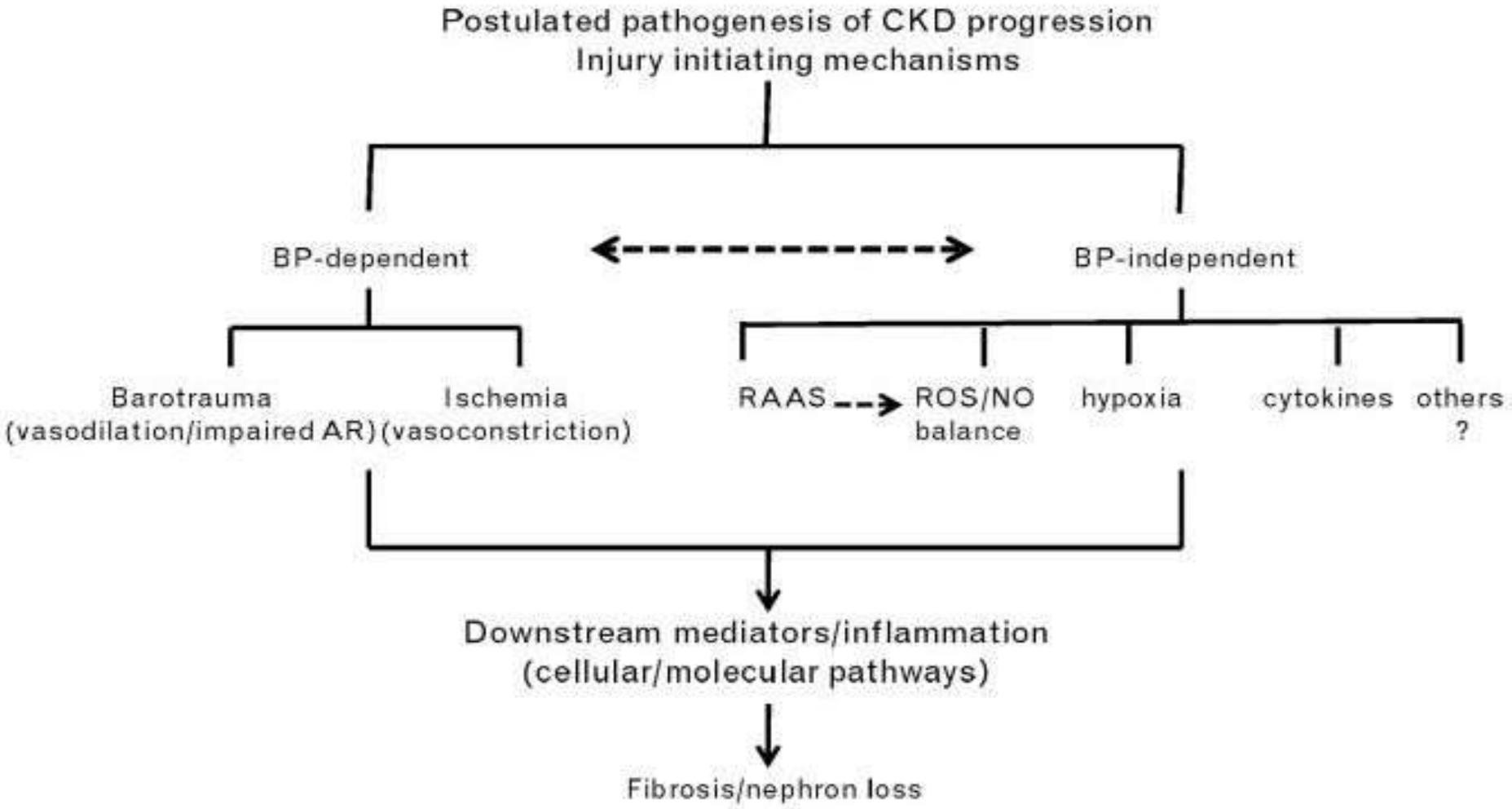


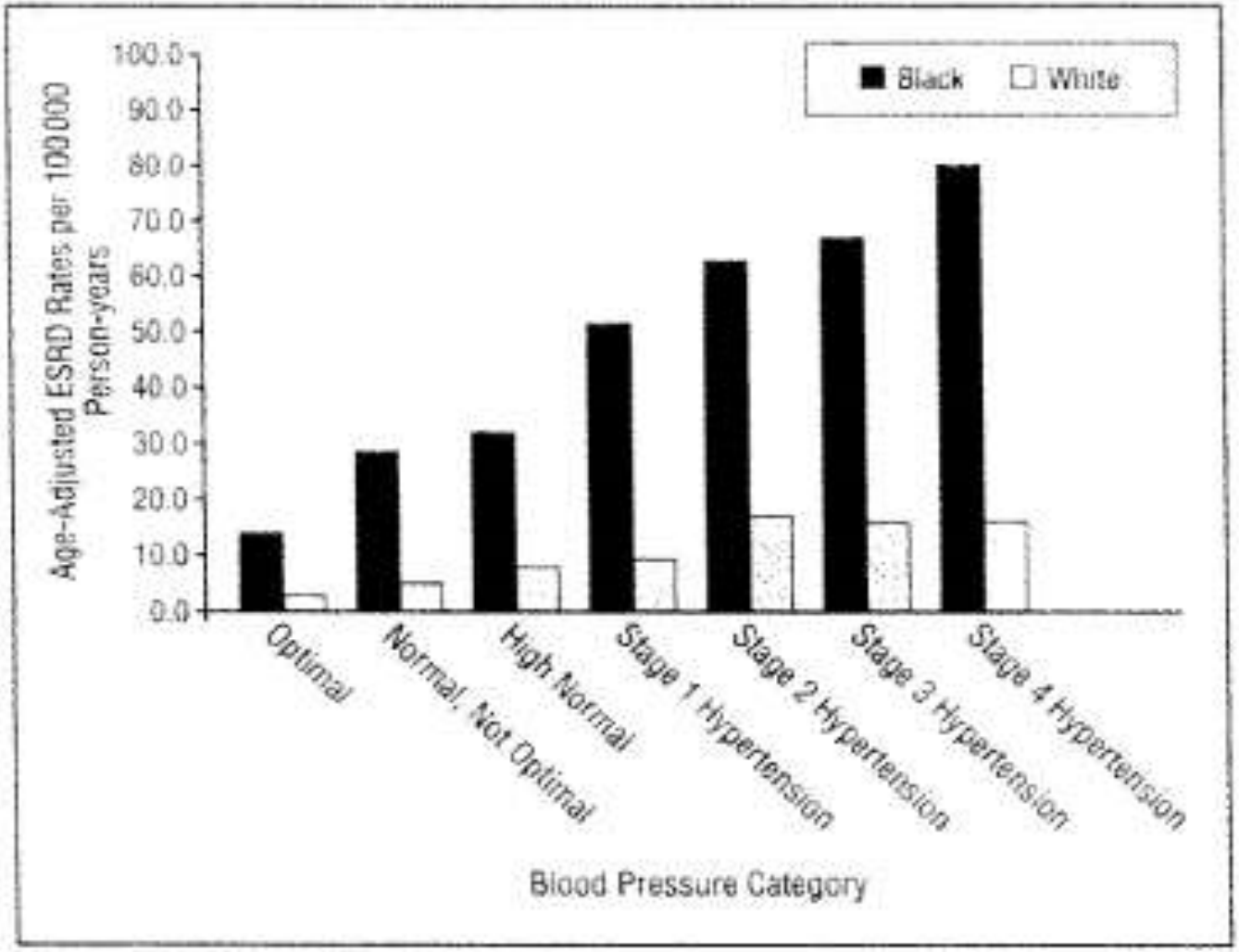
Figure 2. Illustration of the spectrum of pressure flow relationships in the renal vascular bed in hypertension. Pattern A represents the normal renal autoregulatory responses observed in uncomplicated hypertension and shows the constancy of renal blood flow (RBF) despite BP changes within the autoregulatory range. Pattern B indicates the ambient renal vasodilation but preserved autoregulation after uninephrectomy. Pattern C illustrates the impaired RBF autoregulatory responses observed in the 5/6 renal ablation model. Pattern D shows the complete loss of renal autoregulation in 5/6 renal-ablated rats treated with dihydropyridine CCBs. Although RBF is depicted as the dependent variable, the same relationships are expected to obtain for P_{GC}, given that the autoregulatory resistance changes are confined to the preglomerular vasculature.

HTN & CKD progression

Medscape



Risk of ESRD associated with Race



Hsu CY et al, Arch Intern Med 165:923, 2005

OPEN ACCESS Freely available online PLoS one

Association of High Blood Pressure with Renal Insufficiency: Role of Albuminuria, from NHANES, 1999–2006

Methods: We tested the hypothesis that the association between high blood pressure and renal function is modified by albuminuria status by conducting analyses in a cross-sectional study with 12,440 adult participants without known kidney diseases, diabetes or cardiovascular diseases, participating in the National Health and Nutrition Examination Survey (NHANES) 1999–2006.

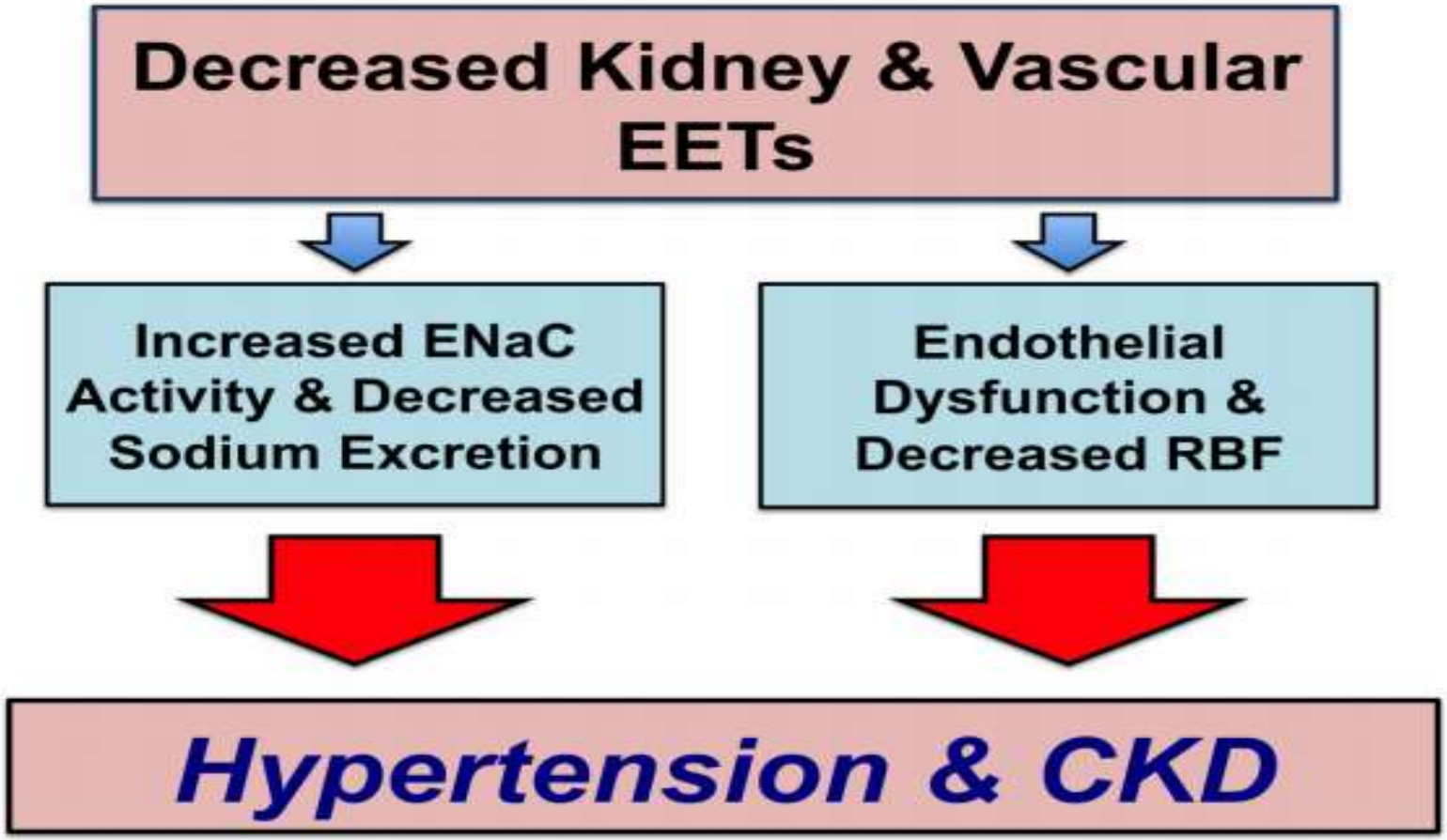
Results: 1226 out of 12440 were found to have unknown high blood pressure and 4494 were found to have reduced renal function. Overall, a moderate association was found between high blood pressure and renal function insufficiency in all participants analyzed. However, among participants with albuminuria, the prevalence of moderate-severe renal insufficiency substantially and progressively increased from normal subjects to prehypertensive and undiagnosed hypertensive subjects (1.43%, 3.44%, 10.96%, respectively, *P* for trend<0.0001); on the other hand, the prevalence of undiagnosed hypertension was also significantly higher among subjects with moderate-severe renal insufficiency than those with mild renal insufficiency (35.54% Vs 19.09%, *P* value <0.05), supporting an association between hypertension and renal function damage. In contrast, no association between hypertension and renal insufficiency was observed among those without albuminuria in this population. Similar findings were observed when the CKD-EPI equation was used.

Conclusions: The association between high blood pressure and reduced renal function could be dependent upon the albuminuria status. This finding may provide a possible explanation for results observed in clinical trials of intensive blood

Hypertension. 2015 March ; 65(3): 476–482. doi:10.1161/HYPERTENSIONAHA.114.03585.

Epoxyeicosatrienoic Acids, Hypertension, and Kidney Injury

John D. Imig



Variants

Hypertension-induced renal dysfunction

- hypertension nephropathy – longterm hypertension causes kidney damage
- ischaemic nephropathy - atherosclerotic changes in macrovessels (altogether with diabetes, hyperlipidaemia).. renovascular hypertension
- vascular nephropathy (nephrosclerosis) – affection of smaller renal vessel causes kidney dysfunction
- renovascular kidney disease – vascular nephrosclerosis + ischemic nephropathy

Epidemiology of hypertension-induced nehropathy (HIN)

- 3rd after ischaemic heart disease and stroke
- RR of kidney dysfunction – 12,5x ↑

Pathology of HIN

- benign nephrosclerosis
- stenosis of renal arteries
- malign nephrosclerosis

A) Benign nephrosclerosis

- in autopsy: 16-18% men and 15-27% women
- clinical follow up: 15% of patients with hypertension
- pathology: thickening of arterial wall, hyalinosis, infiltration of interstitium, interstitial atrophy and fibrosis
- ...smaller kidneys

Clinical symptoms and lab test

- asymptomatic
- nocturia (tubuluinsterstitial changes in concetration)
- early lab findings: microalbuminuria (5-40%), small proteinuria (<1h/day), hyperuricemia, normal renal function
- late lab findings: renal dysfunction,

↑ S-crea, chronic renal failure (3%)

Diagnosis and dif dg

- longterm history of hypertension
- exclusion of other renal diasease
- hypertensive eye changes
- mild proteinuria
- dif dg: ischaemic nephropathy (bilateral renal arterial stenosis), cholesterol microembolization

Treatment

- blood pressure control – 130/80 (125/75)
- diet, salt intake
- ACE inhibitors, sartans, verapamil + other antihypertensive drugs
- intensive treatment of other risk factors (lipids, glycemia)

Hypertension and Kidney Disease: A Deadly Connection

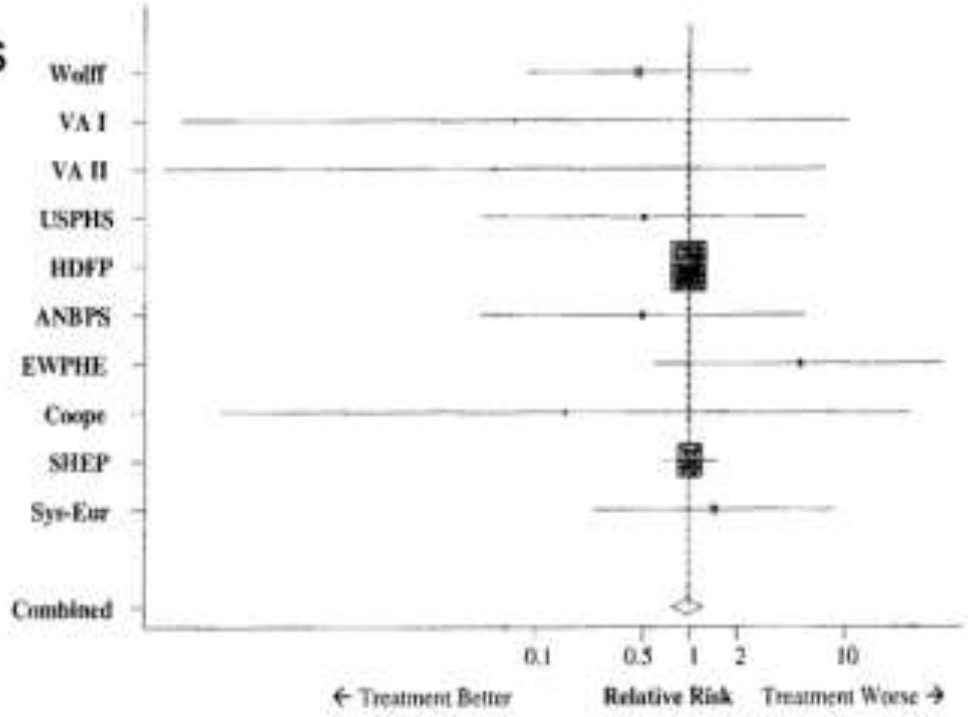
Yousri M. Barri, MD

Table 2. Measures to prevent hypertensive nephrosclerosis

Periodic screening for hypertension
For patients with diabetes
In families with a strong history of hypertension, hypertensive cardiac failure, and hypertension nephrosclerosis
Introduction of diet low in sodium and high in potassium since childhood
Treatment of even mild hypertension
Low threshold for blood pressure treatment
Blood pressure control with drugs patients can afford and tolerate

Effect of Treated Hypertension on Incident CKD

- Major cardiovascular RCTs demonstrate clear benefit for stroke, MI, and heart failure
- Met-analysis with 26,000 patients
- No impact on kidney function



Hsu CY J Hum Hypertens 15:99, 2001

Chia and Ching *BMC Nephrology* 2012, **13**:173
http://www.biomedcentral.com/1471-2369/13/173

BMC Nephrology

RESEARCH ARTICLE Open Access

Hypertension and the development of New onset chronic kidney disease over a 10 year period: a retrospective cohort study in a primary care setting in Malaysia

Conclusions

The rate of decline in glomerular filtration in treated hypertensive patients is comparable to normal subjects. However, the likelihood of patients developing new Stage 3 or beyond CKD over a 10-year period is high. A lower baseline eGFR, hyperuricaemia, presence of diabetes and older age are independent risk factors for the development of CKD among patients with hypertension. These results suggest the need to detect new onset CKD in hypertensive patients, so that appropriate therapeutic strategies can be in place in order to reduce CVD morbidity and mortality in these groups of patients.

Any new TTT?

Hypertension. 2015 March ; 65(3): 476–482. doi:10.1161/HYPERTENSIONAHA.114.03585.

Epoxyeicosatrienoic Acids, Hypertension, and Kidney Injury

John D. Imig

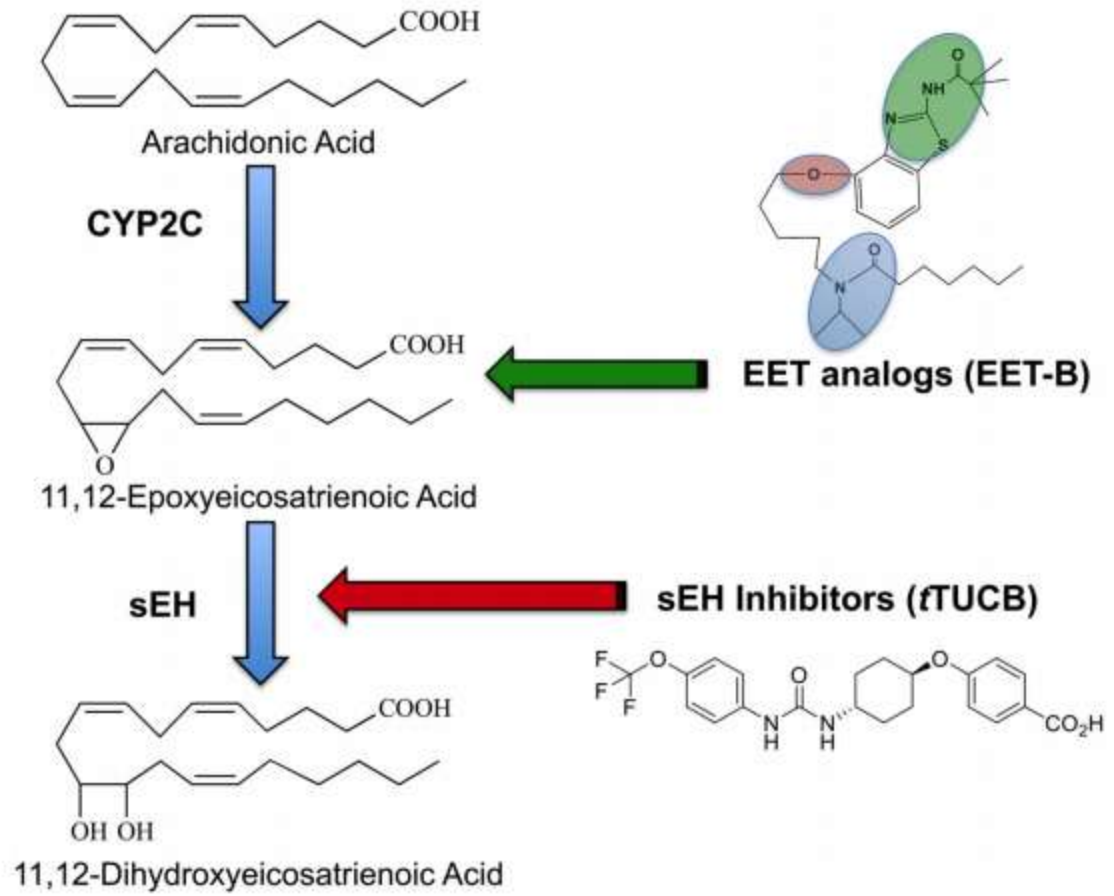


Figure 2. Therapeutic manipulation of epoxygenase metabolites

B) Malignant nephrosclerosis

- rare
- <1% of patients with hypertension (severe)
- pathogenesis – failure of renal vessel autoregulation
- pathology – proliferation endarteritis, fibrinoid necrosis of afferent arteries and capilaries – necrotic glomerulonephritis

Clinical findings and lab tests

- extreme hypertension
- headache, encephalopathy, coma
- neuroretinopathy
- left heart failure
- proteinuria (nephrotic)
- erythrocyturia
- cylinder
- progressing renal insufficiency

Therapy

- therapy of emergent hypertension
- ICU
- i.v. antihypertensives (nitrates, urapidil, labetalol…)
- hemodialysis
- mortality – 30%

C) Stenosis of renal artery/ies

- Hypertension or CKD due to hemodynamicaly significant (>75%) renal arterial stenosis (RAS)... 3%
- Renovascular diseases – renal arterial stenosis with/without hypertension
- Ischaemic nephropathy – renal dysfunction due to renal ischaemia (bilateral RAS)

Renal arterial stenosis - causes

- Atherosclerosis (high age, 80%)
- Fibromuscular dysplasia (younger women, 25%)
- Embole, aneurysm, dissection, malformation
- Arteritis
- Extramural pressure (tumors, fibrosis, uretheral obstruction, cysts…)
- …. RAAS activation

Renovascular hypertension- clinical

- sudden onset, worsening
- + retinopathy
- + negative family history
- + smoking
- + vascular history (IHD, PAD)
- + renal function impairment after ACEi
- + abdominal murmur

Renal arterial stenosis - diagnosis

- Lab: hypokalemia, ↑ aldosterone (secondary hyperaldosteronism), proteinuria, ↑ S-crea
- Ultrasound: renal asymetry (10-15mm), cave bilateral stenosis, IR
- Dynamic renal scintigraphy with enalaprilate
- MRA

Renal arterial stenosis - therapy

- **Aims:**
- hypertension control
- preservation of renal function
- **PTA:** fibromuscular dysplasia and hypertension/renal dysfunction, others?
- **Surgery** (aortorenal bypass): aneurysm, restenosis
- **Pharmacological:** slow titration of ACEi/AT1 (Cave k.i. bilateral stenosis), diuretics, other antihypertensives

D) Ischaemic nephropathy

- ↓ GF due to hemodynamic significant obstruction of blood flow in both renal arteries or in renal artery of solitary kidney or renal failure due to total kidney aperfusion
- atherosclerotic renovascular disease
- atheroembolic kidney disease

Epidemiology

- 15-16% progress to ESRD (3rd after diabetic nephropathy and chronic glomerulonephritis)
- ↑ mortality in dialysis (average survival 27 months)

Atherosclerotic renovascular disease (ARD)

- bilateral renal arterial stenosis – 25-30% patients with renovascular disease
- more frequent in diabetics
- after Tx – 3-10%

Forms of ARD

1) Acute renal failure or Rapidly progressing renal insufficiency

- sudden occlusion of stenotic renal arteries with thrombosis, or embolization
- trias: nephralgia + hypertension + hematuria (+ leucocytosis, subfebrile)
- ↓ poststenotic perfusion after ACEi or sartans
- in 2 weeks after treatment, ARF in 6-10% patients with significant stenosis

Forms of ARD

2) chronic renal insufficiency and failure

- chronic kidney ischaemia due to hypoperfusion in significant renal arterial atherosclerotic stenosis
- asymptomatic.... left heart failure (RAS)
- loss of renal function - ↓ GF 4ml/min/year
- collateral circulation

Diagnosis and dif dg

- progression of renal insufficiency of unknown origin in elderly hypertonic patiens with atherosclerotic history (stroke, MI...)
- rapid and significant impairment of renal function after antihypertensives (not only ACEi, sartans)
- dif dg: acute tubular necrosis, other nehropathies connected with hypertension **(lead poisoning)**

	Hypertension-induced nephropathy	Ischaemic nephropathy
age	40-60	> 60
race	Afroamerican	Caucasian
cause	hypertension	atherosclerosis
mech	perfusion change in HT	hypoperfusion
goal	lowering of BP	stenosis correction
surviv	relatively good	poor

Examination

- ultrasound + doppler
- dynamic scintigraphy (+ enelaprilate)
- MRA of renal arteries
- CTA of renal arteries
- DSA of renal arteries

Therapy

- revascularization - reperfusion!
- bypass
- PTA
- BP control, intervention of risk factors

Atheroembolic kidney disease

- embolization of parts (cholesterol) of atheromatic plaque to peripheral circulation – induction of inflammation
- spontaneous (aneurysm of aorta, anticoagulation therapy)
- after intervention (PTA)
- 0,6-6%

Atheroembolic kidney disease

1) Acute cholesterol microembolization

- suddan lumbal pain, subfebrile
- hypertension, oliguria
- proteinuria, hematuria
- + abdominal (vomitus, ileus, GIT bleeding, spleen infarction)
- + nervous (paresthesia, paresis, amaurosis, TIA)
- + skin (cyanosis, livedo, ulceration of peripheral parts of limbs)

Acute cholesterol microembolization

- diagnosis – difficult
- coincidence with intervention
- impairment of renal function
- eosinophilic leucocyturia
- biopsy (microembolization)
- dif dg: other causes of ARI
- therapy: nephroprotection (hydration, blood pressure control), poor outcome

Atheroembolic kidney disease

2) Chronic cholesterol microembolization

- successive embolization from exulcerated atherosclerotic plaques in elderly sclerotic patients
- successive development and progression of renal dysfunction
- lab: nonsignificant (proteinuria in FSGS)
- ultrasound: aneurysm of abdominal aorta

Conclusion

- Relation between hypertension and renal function reciprocal
- Untreated hypertension leads to renal damage
- Kidney diseases lead to hypertension
- Prevention and therapy – blood pressure control to target
- Inhibitors of RAS, revascularization if possible


MURAKOZE
MESI
dank
RAHMAT
KIE
TÄNAN
BASQUE
GRACES
TAKK
gracias
THANKS
TE
merci
MATONDO
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